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THE TRANSMISSION OF INFORMATION IN PRIMARY RECEPTOR NEURONES AND SECOND-ORDER NEURONES OF A PHASIC SYSTEM

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It is possible to stimulate the pad of a cat in such a way that few, if any, of the primary receptor units of the population under investigation fire more than one impulse. Can information about the size and position of the stimulus be transmitted in the first- and second-order neurones of this system? It is the purpose of the work described in this and two previous papers (Armett, Gray & Palmer, 1961; Armett & Hunsperger, 1961) to answer this question and also the further question, how is the information transmitted in the complete absence of a frequency code?

Mechanical displacements from a Rochelle salt crystal were used to excite the pad receptors. The amplitude and position of these displacements were the only variables considered. The velocity of the displacement was kept well above the critical level, so that the receptor unit threshold was determined solely by the amplitude of the displacement (Armett & Hunsperger, 1961); the area covered by the tip of the stimulator was kept small compared with the receptor unit spacing (see Discussion) and the spread of mechanical events in the tissue (Armett & Hunsperger, 1961). The first problem was to relate these variables, which defined the stimulus, to the patterns of activity in the primary population. Clearly, since there is normally only one impulse in any one unit, any information about the stimulus which is transmitted must depend on activity in a large number of units. The excitation characteristics of single units from the pad were determined by Armett & Hunsperger (1961); in the present paper experiments to measure the number of units active at one time are described. The second problem, the mechanisms which determine the pattern in the primary population, has been considered by Armett & Hunsperger (1961). The third problem is the relation of the patterns of activity in the second-

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order population to the variables defining the stimulus and to the patterns in the primary population. In this paper the second-order cells are those in the dorsal horn (Hunt & Kuno, 1959; Wall, 1960; Kostyuk, 1960; Eccles, Eccles & Lundberg, 1960; Armett *et al.* 1961); cells in the dorsal column nuclei are also second order to these primary units and have been investigated by a number of workers (Amassian & de Vito, 1957; Gordon & Paine, 1960; Kruger, Siminoff & Witkovsky, 1961; Perl, Whitlock & Gentry, 1962), but the observations which are most comparable to those described here are those of McComas (1962; and unpublished). The final problem considered is the mechanism by which the patterns of activity in the primary population set up those found in the second-order population. Experiments are described which provide evidence for convergence of primary units on second-order cells, but none for lateral inhibition. On the basis of this and other evidence, and of some assumptions, a model is proposed; the model is consistent with the behaviour which has been observed in the system.

METHODS

The principal methods have already been described by Armett *et al.* (1961) and Armett & Hunsperger (1961). In summary: decerebrate or anaesthetized cats with low spinal sections were used; records were obtained from single units in the dorsal horn of the spinal grey matter through micropipettes of about 1 μ diameter; mechanical stimulation of the pad was done with two Rochelle salt crystals which could be accurately placed in all three dimensions and the undivided medial plantar nerve was placed over electrodes for electrical stimulation; the lateral plantar nerve was cut.

Procedure. It was necessary to find second-order units in the cord which could be excited by a small mechanical pulse from a crystal applied to the pad. First, the dorsal surface of the cord was explored while the medial plantar nerve was stimulated with electrical pulses of 30 μsec duration. Where the electrical changes were greatest the pia was opened and a series of tracks made through the dorsal horn until the region, in which the early response was maximum, was found (Coombs, Curtis & Landgren, 1956; Fernandez de Molina & Gray, 1957; Armett *et al.* 1961). This region and particularly its medial side was explored until a mass response to mechanical stimulation of the pad was observed. To find such a mass response might involve considerable exploration, though it was usually found somewhere near the region of the maximum activity resulting from electrical stimulation of the medial plantar nerve. The late part of the mass response to mechanical stimulation was usually found first and further exploration was then required to obtain the early part which was more localized. Once the early part of the mass response to mechanical pulses had been found the area was explored carefully until a single unit having a low threshold to a mechanical pulse was found. Units of this kind were not found in all preparations which otherwise appeared to be satisfactory; on the other hand, when the early mass response to a mechanical pulse was found in the first few tracks, then a number of units might be found. The mechanical pulses used in these experiments had a maximum amplitude about 20 μ, a rise time about 0·2 msec and a duration about 0·5 msec. At the end of experiments the electrode was left in place and its position determined (Fernandez de Molina & Gray, 1957).

Recording from the nerve from the pad. The medial plantar nerve was exposed just proximal to the pad for purposes of stimulation. After recordings from the cord had been completed, the nerve was divided proximally and cleaned of excess fibrous tissue. The branch

supplying the medial aspect of the foot was usually cut and separated, as far as was convenient, from the branch coming from the central part of the foot. The crushed end of the latter was fastened to a clean platinum-wire electrode and a second electrode placed at the point where the nerve entered the tissues. In most experiments the nerve and electrodes were then embedded in paraffin wax having a melting point of 39° C. Under these conditions the responses usually remained constant while all records were obtained; all sets of observations, within which quantitative comparisons were to be made, were completed within a few minutes.

RESULTS

The population of primary receptor units

The input to the second-order neurones is the activity in a population of primary receptor units. The activity of individual receptor units, which can be excited by the type of mechanical stimulus employed in these experiments, has been described by Armett & Hunsperger (1961). Further facts are required if the pattern of activity in the population as a whole is to be understood; in particular, one needs to have some measure of the number of units activated under different conditions. If a monophasic record is obtained from a nerve in which all fibres have the same diameter, under conditions in which the diameter of the trunk is small and the inter-electrode distance large compared with the space constant of the fibres, then the area of the response will be proportional to the number of fibres active. The values of conduction velocity given by Armett & Hunsperger, though few, are sufficiently homogeneous to suggest that the area of the monophasic action potentials recorded from the nerve supplying the large pad will, under the recording conditions used, be approximately proportional to the number of active fibres. Even if the relation between the area of the records and the number of active units is not precise, there will only be systematic errors of significance if there is a correlation between fibre diameter and the sensitivity of the receptors; even systematic errors will not invalidate the main conclusions that can be drawn from the results given in this section.

Some fibres from the pad run in a small branch to the lateral plantar nerve (B. C. M. Williamson, personal communication). It appears that these are probably confined to the lateral lobe of the pad. In practice the experiments described here were restricted to the main central part of the pad.

The responses to various amplitudes of a mechanical pulse. The relation between the area of a monophasic action potential found in the whole nerve from the pad, and the amplitude of a displacement of the mechanical stimulus, is shown in Fig. 1. This graph is, in general, typical of those obtained in eleven other preparations. In this experiment the smallest response which could be obtained was seen to come and go in a perfectly all-or-nothing manner, and may therefore be assumed to be the response of a single unit. The ordinate scale is given in multiples of the area of this

smallest response. If the area of the monophasic record is assumed to be proportional to the number of active fibres then a stimulus with an amplitude of displacement of about 20 μ was exciting about 50 units. The technical difficulty of this type of experiment is that all the fibres in the nerve must be kept functional if the bulk of the active units is to be observed; it is never complete because of the small proportion of the units which run in the lateral plantar nerve. However, unless the nerve is cleaned and unwanted bundles of fibres from other parts of the foot cleared from the branch from the large pad, the signal-to-noise ratio is unlikely to be good enough to detect the activity of a single unit. In only one other preparation was an undoubted single unit response detected and

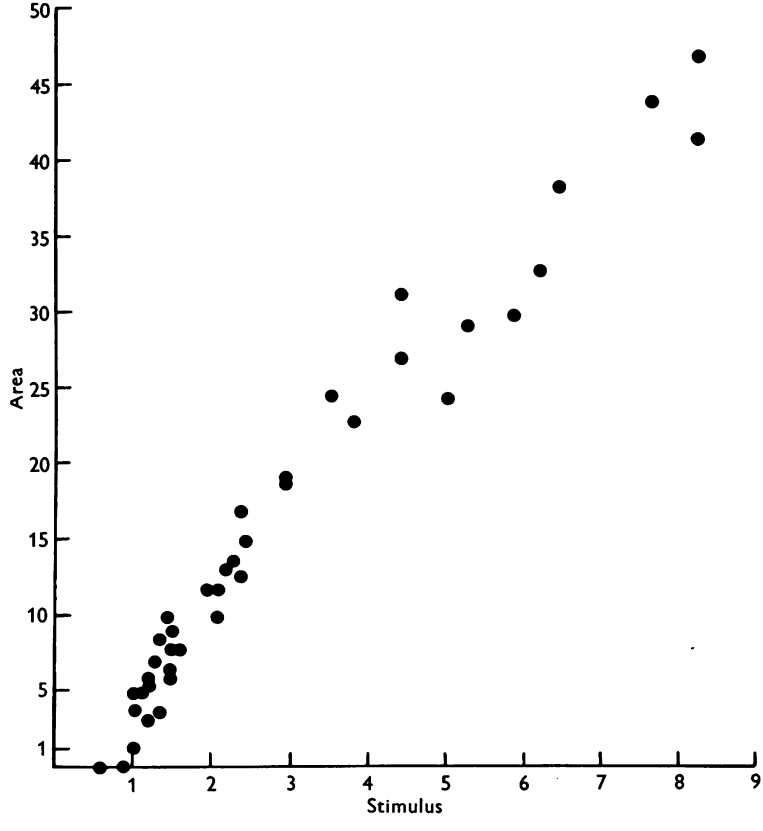

Fig. 1. Relation between the amplitude of the displacement of mechanical pulse applied to the large pad and the area of the response recorded monophasically from the whole nerve from the pad. Abscissa: displacement amplitude given in multiples of that required to excite the lowest threshold unit; the largest stimulus was about 20 μ. Ordinate: area of the response given in multiples of that of the smallest response (this was all-or-nothing).

in this instance the maximum area of response was 18 times that of the all-or-nothing quantum. In 4 of the other 10 experiments the maximum area was more than 10 times the smallest observed area; 25, 16, 16 and 10 times. It is justifiable to conclude from these experiments as a whole that there is a graded relationship of some form between the amplitude of a displacement applied to the pad and the number of primary receptor units activated, and that the maximum number of units activated is in the order of magnitude of tens.

Time course. The time course of the monophasic action potential recorded from the nerve from the pad is significant in determining the patterns of

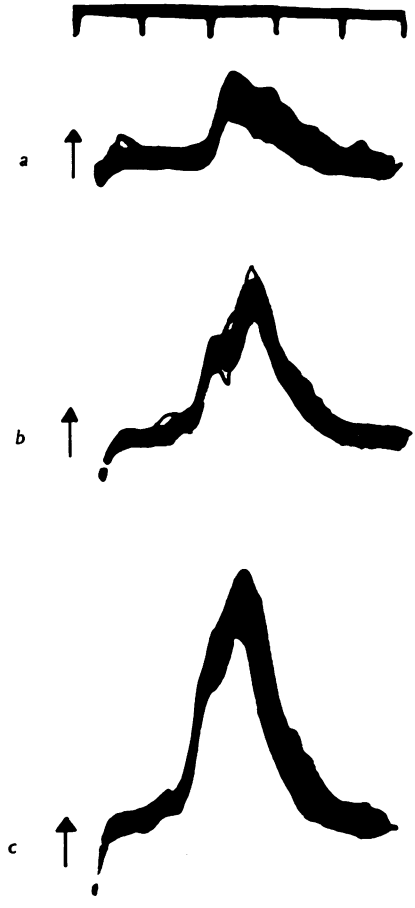

Fig. 2. Monophasic action potentials recorded from the nerve from the pad in response to stimulation of the pad with a brief mechanical pulse. The following displacement amplitudes were used, given as multiples of that required to excite the lowest threshold unit: *a*, 2·1; *b*, 3·8; *c*, 8·2. Time marker, msec. The start of the pulse is indicated by the arrows. Same experiment as Fig. 1. Superimposed traces.

activity in the population of primary receptor units (see Discussion). Figure 2 illustrates typical records. These are of superimposed traces and the thickness of the trace during the activity compared with the thickness of the base line gives a rough indication of the stability of the response. The total duration of activity was normally between 2 and 3 msec; in one experiment a small additional wave was seen after the main response.

Recovery after a response. It is known from the studies on single primary units (Armett & Hunsperger, 1961) that there are a number of factors which determine the excitability of a unit at various times after a conditioning pulse has been applied to the pad. These include the summation of receptor potentials, the depression of the receptor potential, refractoriness and mechanical interactions which appear to be the result of interference between travelling mechanical waves.

The response of the whole population to a test pulse has been observed at different times after a conditioning pulse in three different experiments; the stimuli were applied at different points in two of these, in the third both pulses were delivered through the same crystal. In each instance the extra area added to the monophasic record of the response to the conditioning pulse, as a result of applying the test stimulus, was calculated as a percentage of the area excited by that test pulse on its own. The results in all experiments were consistent, and the most important point is that recovery was complete in 4–5 msec. When the two pulses were simultaneous the test pulse added to the total those units not fired by the conditioning pulse but which could be fired by the test pulse; probably it also added some units not fired by either alone but which could be fired by a process of summation. The test stimulus added least to the total when it was delayed 1–2 msec. The main factor in determining this minimum was probably the mechanical one (Armett & Hunsperger, 1961); none the less at this time summation of receptor potentials would be less effective than with simultaneous pulses, while recovery from refractoriness would hardly have started.

Second-order receptor neurones

Typical records obtained from the dorsal horn in response to an input such as that described in the last section are shown in Fig. 3. In all, 43 units were found which responded to a single mechanical pulse from a crystal to the large pad and were, in other respects, usable. Of these some were seen to respond to electrical stimulation of the medial plantar nerve with a latency that placed them in the short-latency group of Armett *et al.* (1961); these authors gave reasons for supposing these cells to be second order to mechanically excitable afferent units conducting at about 60 m/sec (see also Fernandez de Molina & Gray, 1957); this conduction velocity was

that found for the receptor units in the pad studied by Armett & Hunsperger (1961). Other units, whose activity was obscured during electrical stimulation of the medial plantar nerve, were identified as belonging to this group by their time relation to the mass response set up on mechanical stimulation (see below). The results described in this section refer only to units which could be reasonably assigned to this group of cells; 34 units fell

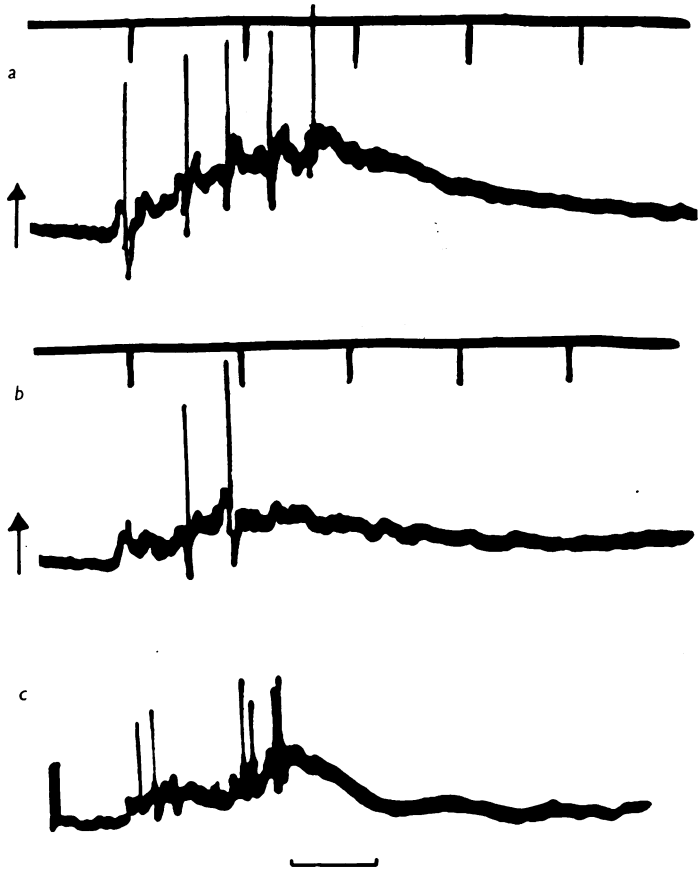

Fig. 3. Examples of response of the dorsal horn to stimulation of the pad with mechanical pulses delivered at 1/sec. *a* and *b*, two records from the same run; the stimulus (↑) in *a* was 1·2 × that in *b*; time marker, 10 msec. *c*, another experiment; time bar, 10 msec.

into this category, and it will be seen from Fig. 4 that the 26 of these units which were located histologically, were found in the same region as the short-latency units described by Armett *et al.* (1961).

The records shown in Fig. 3 consist of two distinct responses; the spikes are the responses of single units, while the slower potential changes from which they arise are mass responses; these slower potentials are a resultant

of the activity of cells in the neighbourhood of the electrode. In all these records and those of Fig. 5 the mass response begins relatively sharply at about 7–8 msec after the stimulus and reaches its first small peak within a millisecond. This early peak has been compared with the monosynaptic phase of the mass response to small electrical stimuli, adjusted to give responses of about the same size. The time course of the two responses was very similar and the greater latency of the mechanically excited response could be accounted for by the time between the mechanical pulse and the arrival of an action potential at the electrode position (cf. Fig. 2).

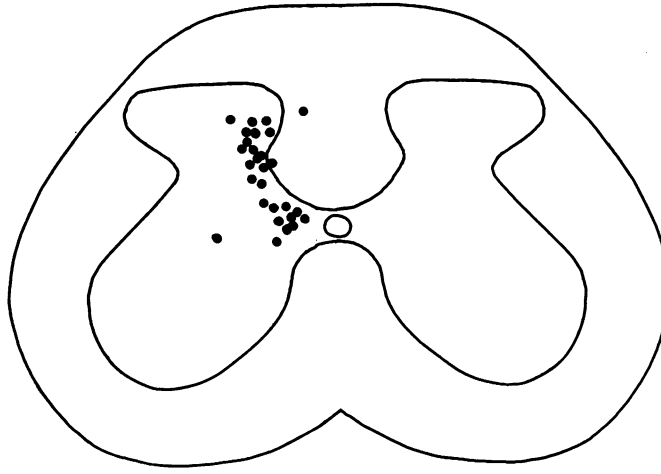

Fig. 4. Composite diagram of the spinal cord. Each point indicates the position of a second-order unit which was excited by a mechanical pulse to the pad. The points were placed on the diagram so that they had, as far as possible, the same relation to the main features of the cross-section as they had in their own cord. These points were obtained by a co-ordinate method and the position of individual points is not very accurate.

The time course of the activity in Fig. 3, which is typical for low repeat frequencies, also shows marked late activity. This late activity, unlike the early phase, disappeared on stimulation at 10/sec (Fig. 5) and was more widespread in the cord than was the early phase (see Methods). The late activity appeared to be more marked in decerebrate than in anaesthetized animals, though all had spinal sections. The early phase appears to be associated with the monosynaptic activation of the cells by primary units conducting at about 60 m/sec. The late activity might be due to impulses conducted in much smaller fibres, impulses which might have been missed by the techniques used by Armett & Hunsperger. The late activity can, however, be entirely explained by the activation of fast fibres. The mass responses to very small electrical stimuli given at low repeat frequencies

lasted as long as and were very similar to those obtained with mechanical pulses. In three experiments single units, which gave prolonged responses to mechanical stimulation, could also be excited to the same level of activity by small electrical stimuli; that is, stimuli giving mass responses as small as those produced by mechanical pulses. The responses of these units could last as long after electrical stimulation as after mechanical.

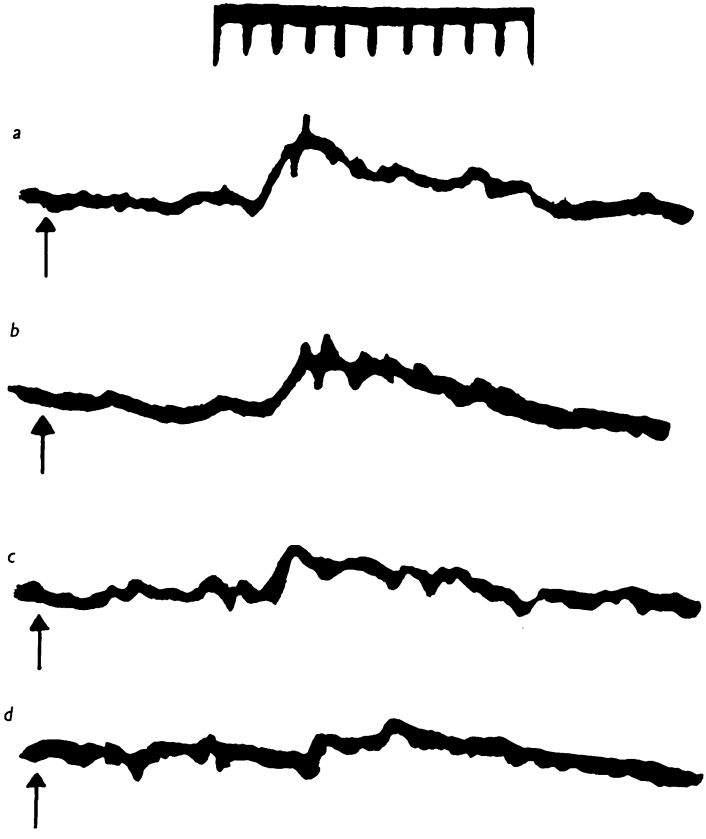

Fig. 5. A series of records of the early mass response to mechanical stimulation of pad at 10/sec. The values of stimulus strength in arbitrary units were: *a*, 11·0; *b*, 9·5; *c*, 8·0; *d*, 6·5. Time marker, msec. Note different time scale from Fig. 3. The start of the pulse is indicated by the arrows.

The responses to both types of stimulation changed in the same way with changes in repeat frequency and stimulus strength. Only the largest fibres can have been excited by the electrical stimuli and the results can therefore be entirely explained in terms of the activation of these large fibres, which are the only ones known to be activated by the mechanical pulses used.

The relation between stimulus strength and size of response

The mass response of the cord to mechanical stimulation of the pad. When the pad was stimulated with mechanical pulses at frequencies of 1/sec and less, all parts of the mass response, on the average, increased in size as the amplitude of the stimulating displacement increased. In all experiments there tended to be large fluctuations at any one stimulus strength and these fluctuations were greatest in the later parts of response. In some experiments the scatter was much greater than any increase of size which occurred systematically with increasing stimulus strength; in others there was an undoubted relation between these variables. The results of measuring mass responses were in fact very similar to the results obtained by counting the number of impulses fired by a single cell (cf. Fig. 7).

When the pad was stimulated at 10/sec, only the early activity appeared. Figure 5 shows this activity related to stimulus strength. These responses were stable.

This early response is graded, and it is therefore clear that the information which is found in the primary population about the amplitude of a stimulus is passed in some form to the second-order cells. This type of measurement cannot distinguish between the grading of activity in a single cell, e.g. synaptic potentials, and variations in the number of units active.

The response of single units in the cord to electrical stimulation of the primary units. The output of the second-order cells, in the form of nerve impulses, can be shown to be related to the number of active units amongst the primary population. This is most clearly shown by electrical stimulation of the medial plantar nerve. Electrical stimulation of the nerve presumably excites many more fibres than does a mechanical stimulus to the pad; the size of the early mass response to electrical stimulation of this particular nerve (Armett *et al.* 1961) is very much larger than can be obtained by mechanical stimulation (Fig. 5). Other differences between electrical and mechanical stimulation can also be turned to advantage; an increasing electrical stimulus will bring in fibres in order of their diameter, but with no regard to their organization; a mechanical stimulus does the reverse.

Figure 6*a* is a plot of the number of impulses against the peak voltage of a 0·5 msec duration electrical pulse at a stimulation frequency of 10/sec. This shows that the impulse output can be graded when the repeat frequency is at 10/sec. Figure 6*b* was taken at 1/sec. It also differs in that the abscissa is plotted in terms of the area of the record of the incoming volley taken from the dorsal root. Figure 6*b* shows that a considerable increase in the response was observed when the input was increased from nothing to 30% of maximum; that is, when only the larger fibres were

stimulated. Figure 6*a* shows that about 70–80 % of the increase in the number of impulses occurred within the first 30 % increase in stimulus strength above threshold. The results over this range have been consistent, and are in agreement with the mass response results of Fernandez de Molina & Gray (1957).

The response of single units in the cord to mechanical stimulation of the pad. The responses of single cells to stimuli applied at frequencies of 1/sec and less were very variable. Two examples are illustrated in Fig. 7: of these one is an example in which no relation between the number of impulses and the stimulus strength could be observed; in the other there is clearly a relation between the two quantities, even though the scatter is large. It is apparent from these examples that under such conditions little information can be transmitted by the number of impulses fired by any one unit.

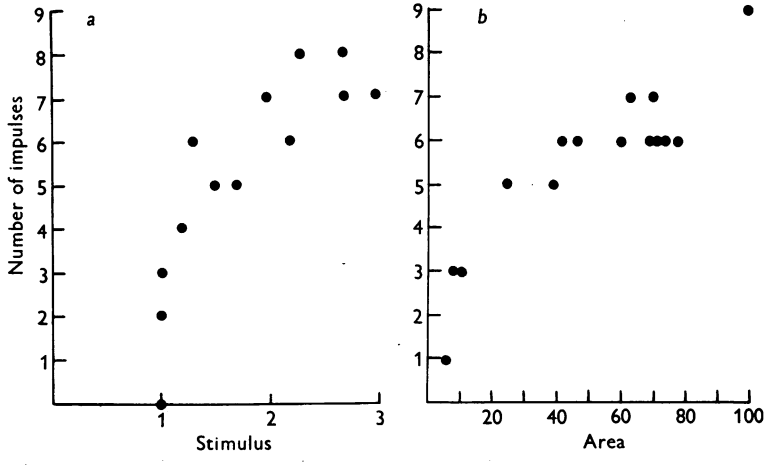

Fig. 6. The response of units in the spinal cord to electrical stimulation of the medial plantar nerve. *a*: abscissa, peak voltage of a 0·5 msec duration pulse given as multiples of threshold; ordinate, number of impulses; stimulus frequency 10/sec. *b*: abscissa, area of incoming volley in a dorsal rootlet as a percentage of the largest area obtained; ordinate, number of impulses; stimulus frequency 1/sec.

There is reason to suppose that the response of the second-order population to a mechanical pulse involves an appreciable number of units. If this is so, the relation between stimulus strength and the total number of impulses might still make a significant contribution to the amount of information transmitted. For this reason all the observations were pooled and the linear correlation was worked out. A correlation, albeit a poor one, exists (correlation coefficient = 0·51, S.E. of correlation coefficient = 0·05). The relation is shown in Fig. 8, in which the mean number of impulses is plotted for each group of stimulus strengths.

At repeat frequencies of 1/sec and less not only was the response variable with a constant stimulus, but the threshold value for a single impulse fluctuated. It was usually difficult to obtain any consistent value of threshold in such experiments. This can be illustrated by the following figures; they are the ratios of the largest values of a single stimulus at

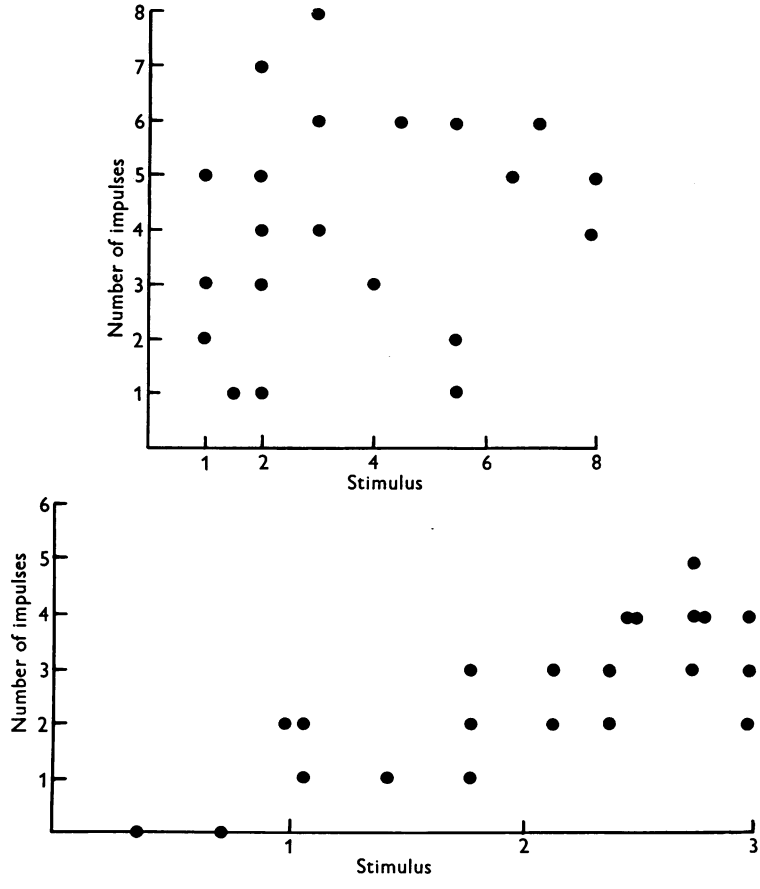

Fig. 7. The response of units in the spinal cord to mechanical stimulation of the pad at 1/sec. Abscissa; amplitude of the displacement given as multiples of threshold. Ordinate; number of impulses. Two different units. Each dot is one observation.

which no response was obtained to the smallest value to which a response occurred; both were taken within a period of 10–20 sec; 2, 3·1, 1·8, 2, 5·7, 4·7, 1·04, 2·3, 2·3. In six of these the smallest stimulus which gave an impulse was about 1–3 μ; that is about the same as required to excite the most sensitive primary units (see Armett & Hunsperger, 1961).

At repeat frequencies of 10/sec the situation was different. The number

of impulses fired by the largest stimuli was always small and often only one. The consistency of the response was, however, good. This may be indicated by the stability of the threshold, in terms of the amplitude of the applied pulse. In four experiments in which repeat measurements were made over periods of about 1–2 hr the coefficients of variation of the whole of each series of values of threshold were: 3 % (number = 15), 22 % (9), 9 % (30),

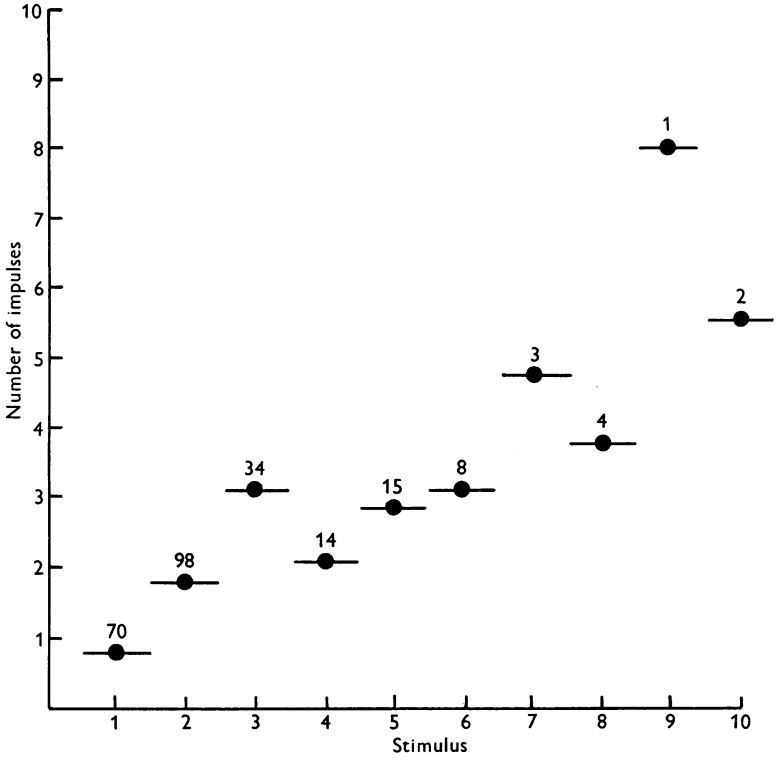

Fig. 8. The average number of impulses fired at different strengths of mechanical stimulus at 1/sec. Abscissa; displacement amplitude in multiples of threshold. Ordinate; number of impulses. The bars indicate the range of stimulus strength over which the results have been averaged and the numbers above them the number of observations.

6 % (18). These figures indicate the long-term stability of the system. The observations from which these figures are derived were made in groups of three, each group taking perhaps 5 min; thus some estimate of short-term stability may be given by the root mean square of the deviations of each individual observation from the mean of its group. The corresponding figures, expressed as a percentage of the over-all mean, are 2, 11, 2, 4 %, respectively. The actual value of the threshold amplitude was com-

pared in 8 experiments with that of the primary units of the same preparation (see last section of Results for details, p. 410). Thresholds of second-order units ranged from 2·8 to 8·5 times the lowest threshold primary units. The estimated numbers of primary units active (see above) at the threshold of the second-order neurone ranged from > 2 to 32.

The receptive fields

Five receptive fields were measured in full and the measurement of others was attempted. The difficulty of these measurements was that the unit had to be held while the stimulator was adjusted at every point to have the same resting level in relation to the surface. The satisfactory results that were obtained showed large variations in area; the smallest had an area of about $2{\cdot}5 \times 1{\cdot}5$ mm while the largest was of the order of 9×9 mm. These areas are defined in the same way as was used by Armett & Hunsperger (1961) in describing the receptive fields of first-order units; that is, it is an area from which a response can be obtained with the particular stimulus employed. The maximum stimulus used in these experiments was the same as that used by Armett & Hunsperger and the results are therefore comparable. The variations found here and among first-order receptive fields (25–120 mm^2) are such that only a very large series of observations would give any significant results. It may be noted, however, that the smallest fields of the second-order units were smaller than the smallest found for primary units.

In all the fields investigated there was a central area in which the threshold of the second-order cell remained constant within the limits of error or varied relatively little. Outside this central area the threshold increased as the distance from the centre increased. In one experiment the area of the monophasic record from the nerve from the pad was measured for each position, the size of the pulse being always that which was just-threshold for the second-order cell. All the stimuli were equivalent in respect of the second-order cell, but it was found that fewer primary units had to be excited in the centre of the receptive field than at the periphery. This means that not all fibres from the pad are equally effective in contributing to the excitation of any particular second-order cell. It may mean that some are effective and others not or that there is a gradation of effectiveness that decreases with distance from the centre of the receptive field.

Responses to two mechanical pulses

To explain the responses of the second-order cells we need information about the convergence of primary fibres on to these cells. In particular we need to know whether there are only facilitatory connexions or whether inhibition can be found when stimuli are applied at a distance apart.

Furthermore, we need to know how long any effects may last. This type of information may be obtained by conditioning a cell with a mechanical pulse applied at a certain point, and then testing the excitability of the cell with a test pulse applied after a certain time at another point. It must be remembered that it is the excitability of the cell which we wish to test. This might be measured by knowing the number of active primary units converging on the cell as a result of the test pulse. We do not know this directly because, as has been shown by Armett & Hunsperger (1961), the excitability of the receptors in the pad is altered after a conditioning pulse. However, we can measure the area of the monophasic action potential set up in the nerve from the pad as a result of a mechanical stimulus. The reasons which justify relating this area to the number of active fibres in the nerve have been considered in an earlier section. If the excitability of a second-order cell is, under suitable experimental conditions, linearly related to the number of fibres active in the nerve from the pad, then the area of this monophasic action potential can be used as a measure of cell excitability. This assumption is believed to be justified for the following reasons. In the central area of the receptive field of each cell the amplitude of displacement required to excite the cell changes little; units from this area are therefore presumably (on the average) equally effective in exciting the second-order cell. If the test stimulus is kept at one point in the most sensitive region and the strength kept at or below that required to excite the cell, only primary units of equal (average) effectiveness will be excited. The contribution of the conditioning stimulus to the excitability of the cell is only measured in terms of the number of primary units excited by test stimuli and therefore the position and strength of the conditioning stimulus need not be considered. In view of this argument the following procedure was adopted, in order to obtain an estimate of the number of active primary units converging on the cell as a result of the test stimulus and hence of the excitability at that time.

The minimum amplitude of a mechanical test pulse required to excite a second-order cell was found. This threshold was found for the test pulse both alone and at various times after the mechanical conditioning pulse. The test pulse was always applied at the same point in the region of maximum sensitivity, while the conditioning pulse was moved to a series of different positions. The threshold to the test alone was measured immediately before every conditioned observation. The size of these test pulses used alone varied little and actual variations have been quoted above. All measurements were made with a stimulus frequency of 10/sec in order to obtain a sufficiently high stability. After measuring the thresholds under all required conditions the nerve from the pad was prepared for monophasic recording. Each combination of test and conditioning

pulses was then repeated, keeping the amplitude of both pulses, the timing and the distance apart exactly as they had been when the threshold of the cell was measured. The area of the response to the test pulse alone will be referred to as N_∞. This value is related to the number of primary units activated by the test pulse alone, and is a measure of the activity which must be added to the resting cell for it to reach threshold. When a conditioning pulse was given as well as a test, the total area of the response was

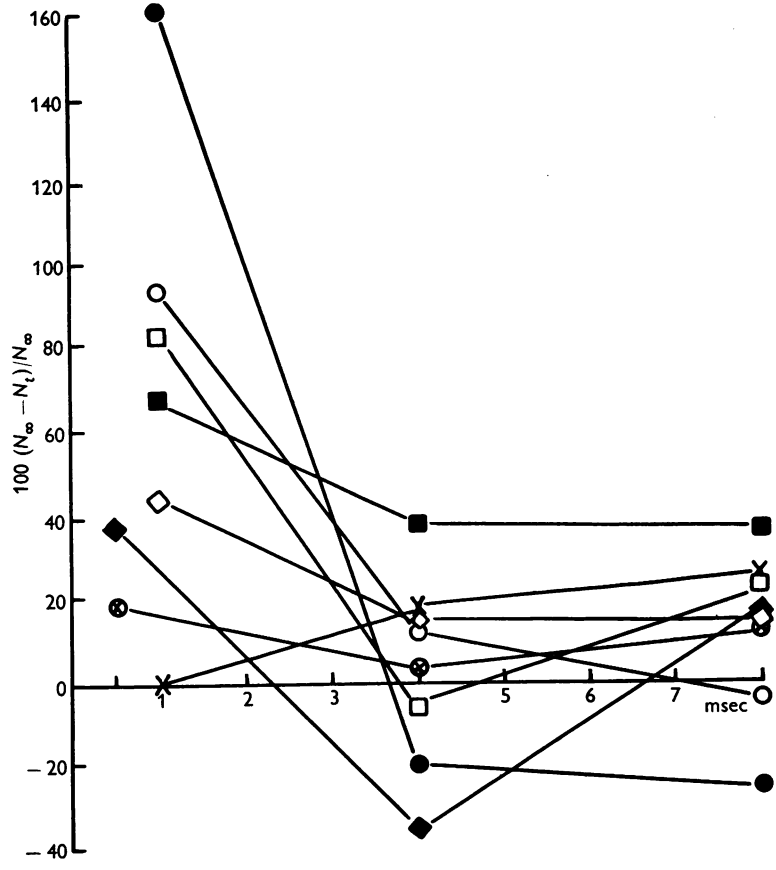

Fig. 9. Interaction of primary receptor fibres on a second-order cell. Abscissa; time after a subthreshold conditioning pulse at which the test pulse was applied. Ordinate; a measure of the contribution of the volley set up by the conditioning pulse to the excitability of the second-order unit; this measure is $100(N_\infty - N_t)/N_\infty$, where N_∞ is an estimate of the number of fibres activated by the threshold test pulse alone and N_t is an estimate of the number of extra fibres activated by the threshold test stimulus at time t after a conditioning pulse. Distances between stimuli: ◆ = 1·5 mm, ⊗ = 2·5 mm, ■ = 3·0 mm, ◇ = 5·3 mm, ○ = 6 mm, × = 7·8 mm, ● = 8 mm, □ = 10 mm. Conditioning stimulus approximately 90 % of threshold. For further information see text.

measured and from this was subtracted the area of the response to the conditioning pulse by itself. This difference, referred to as N_t, is related to the number of extra primary units added by the test pulse to those already excited by the conditioning pulse. N_t will be a measure of the activity required to bring a conditioned cell to threshold. The difference between N_∞ and N_t is thus a measure of the contribution to the excitability of the cell that has been made by the conditioning pulse at that particular time and place; this estimate of the excitability change is in this way expressed as the number of fibres which would have to be excited by the test stimulus to bring about the same change in excitability. The difference has been given as a percentage of the value of N_∞, so the actual quantity plotted has been $100(N_\infty - N_t)/N_\infty$. Positive values of this function indicate facilitation, since the input required to excite the cell is less after conditioning than without it. Negative values indicate inhibition because a larger input is required after conditioning.

The results of such an experiment are given in Fig. 9 in which

$$100(N_\infty - N_t)/N_\infty$$

is plotted against the time interval for a number of different positions of the conditioning pulse. The errors involved in measurements of this kind are inevitably high and account for most of the scatter in Fig. 9 and the value $> 100\%$. No conclusion can be drawn from a single experiment. The results from 12 such experiments have therefore been pooled. The values were grouped into three time intervals and the means and standard deviations found. Figure 10 is a graphical display of this information. There can be no doubt that there is a significant excitatory contribution of a conditioning stimulus at short intervals and, in this figure, there is certainly no suggestion that there is any inhibitory effect at any time. The three groups were then subdivided by distance; four subgroups of each time group were considered, 0–3, 3–6, 6–9 and 9–12 mm. In the subgroups at 9–12 mm the means were near zero, but the numbers were very small and no significance can be attached to them. Of the other nine subgroups, all those at 0–3 msec had mean values of $100(N_\infty - N_t)/N_t$ greater than 47 % and they all differed from zero by more than three times the standard error of the mean, and of the remaining six subgroups only one mean was negative (-8%, S.E. 12 %). There is therefore no evidence of lateral inhibition at this level at any distance on the pad and at any interval up to 9 msec.

DISCUSSION

Can information about the size and position of a stimulus be transmitted in the first- and second-order neurones of the system considered? The answer must be 'yes' for all parts of this question; the second-order cells have been shown to produce responses which are graded with the ampli-

tude of the mechanical stimulus and also some second-order cells have been shown to have small receptive fields. The second question posed in the introduction—how is the information transmitted?—is considered in the rest of the discussion. In the first part patterns of activity in the primary population are reconstructed. In the second part the patterns of activity in the second-order cells are discussed in relation to the amplitude and position of the stimulus. The third part presents a model, which is based on certain findings, is consistent with the results obtained and which provides a possible explanation of how the pattern in the primary population is related to that in the second-order population.

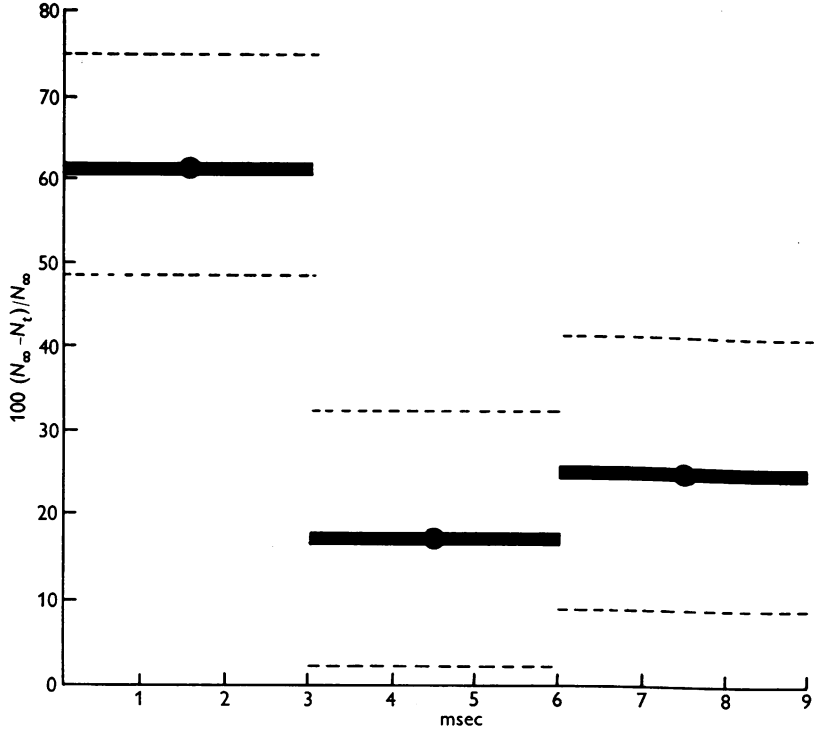

Fig. 10. Mean values of experiments such as those of Fig. 9. Co-ordinates as in Fig. 9. The length of the bars indicates the times over which the results have been grouped. The interrupted lines indicate plus and minus twice the standard error of the mean.

Patterns of activity in the primary units

A model (Fig. 11) has been constructed from the observations made by Armett & Hunsperger (1961), and this has been checked against the observations described in this paper. The area of the pad is about 120 mm^2; the maximum number of units fired by a single pulse was estimated at

about 50 and the number of fibres which come from the pad and have diameters consistent with the conduction velocities given by Armett & Hunsperger has been found by B. C. M. Williamson (unpublished) to be 50–100. An area of 1·5 mm^2 per unit has therefore been taken and the assumption made that every unit is equidistant from its immediate neighbours. This leads to an arrangement such as that in Fig. 11*f*, which has a total of 61 units, a receptor spacing of 1·3 mm, and an area approximately that of a pad. The range of thresholds of the receptors is given by Armett & Hunsperger as approximately a factor of 10; part of this is probably due to the condition of the horny layer of the pad and three thresholds are

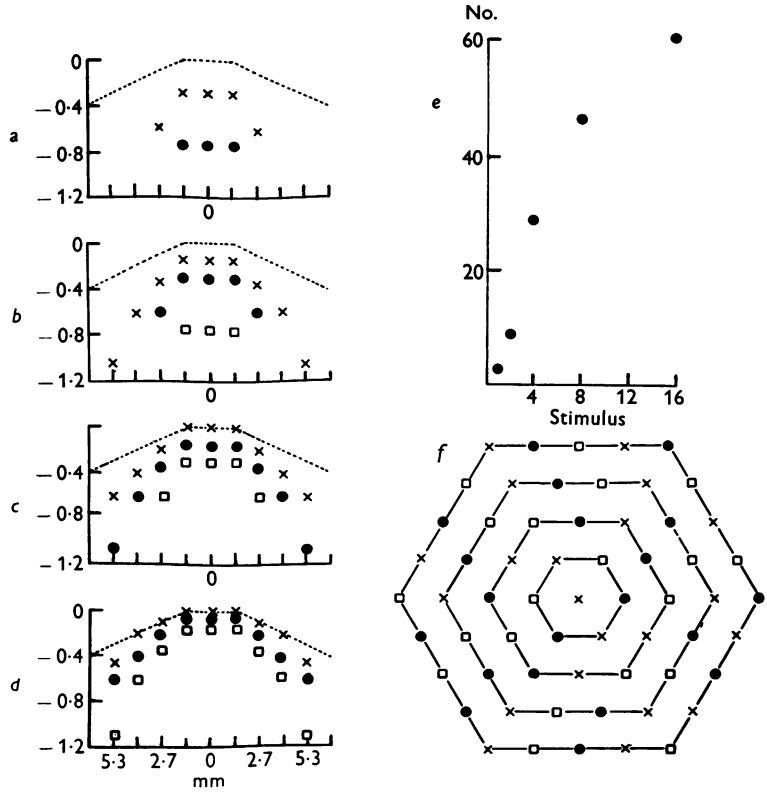

Fig. 11. Model to illustrate distribution of activity in the primary population. *a–d*; time lag behind stimulus in the initiation of an impulse (ordinate) for units centred at different distances on either side of the point of application of the pulse (abscissa); stimulus strength, *a* = twice; *b* = 4 times; *c* = 8 times and *d* = 16 times threshold of the most sensitive unit; symbols indicate units with different thresholds × = 1×, ● = 2×, and □ = 4×. *f*; assumed distribution of these units on the pad around a central stimulus. *e*; relation, in the model, of number of units active (ordinate) to stimulus strength in multiples of threshold (abscissa). For details see text.

therefore indicated ($\times$ = 1, ● = 2 and □ = 4). The centres of the receptive fields had an area of uniform threshold and in the model it is assumed that this extends over a distance of one unit in each direction. The increase in threshold outwards from this point appears to be due to the attenuation of a mechanical wave; Armett & Hunsperger give a figure of 2 mm for attenuation of the wave to half amplitude and this has been used, assuming an exponential decay. The mechanical wave travels at a velocity of about 13 m/sec, and this causes a delay in the excitation of units at a distance from the stimulus. Figure 11*a–d* indicates the calculated times at which impulses will occur at different distances on either side of the stimulus for units having the different thresholds indicated by the symbols. Each part of the figure indicates a different value of stimulus strength. The dotted line in each part of the figure indicates the delay due to the time taken for the mechanical wave to spread and the further delays behind this line are due to the latency required for impulse initiation as given in Fig. 7 of Armett & Hunsperger (1961). From the arrangement in Fig. 11*f* and the values given in *a–d* it is possible to calculate the number of units that will be activated at any given stimulus strength, and a number of these are given in Fig. 11*e*. These are consistent with the values shown in Fig. 1.

It is also possible to calculate the time distribution of the activity and hence the shape of the monophasic action potential. This has been done by taking as the basic unit the time course of a monophasic impulse of conduction velocity of 60 m/sec from Gasser (1941). One other factor was introduced at this point; Armett & Hunsperger showed that some units responded to one phase of the mechanical wave in the pad and others to the opposite phase. This leads to units of one group having latencies 0·5–1 msec longer than the other. A value of 0·7 has been taken and it has been assumed that the units fall equally into the two classes. Reconstructed monophasic action potentials are shown for three values of stimulus strength in Fig. 12; all values of amplitude have been adjusted so that the peak height of Fig. 12*c* is the same as that of Fig. 2*c*. It may be noted that the peaks seen in Fig. 2 are a regular feature of such records. The agreement between the observations and the model is such that the model may be regarded as consistent with the facts.

In the type of system just considered many units are involved in the transmission of information about the amplitude and position of a movement at a single point. Natural stimuli are usually much more complex and require information about movements at many points to describe them. In this system there are not sufficient primary units to transmit complete information about many such movements at one time. The information is, however, transmitted rapidly and the population has returned to its resting state in about 4 msec. It would be possible for a

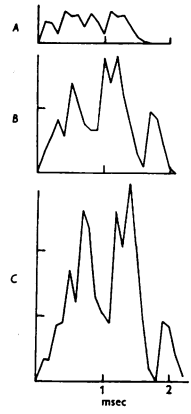

Fig. 12. Monophasic mass action potentials calculated from the model illustrated in Fig. 11. *a*, twice; *b*, 4 times; *c*, 8 times threshold. For details see text.

single unit to take part in the transmission of information about 250 different movements at discrete points every second; this could happen when the pad is moved across a surface.

Patterns of activity in the second-order cells

The purpose of this section is to consider the relation between patterns of activity in the second-order population and the magnitude and position of a mechanical stimulus. The immediate input to the cells is the activity of the primary population. Patterns of activity in large fibres have been considered in the last section; there is no evidence that smaller fibres are excited by the stimuli used (Armett & Hunsperger, 1961) and evidence has been given above showing that all the activity observed could be accounted for by the input from the large fibres.

Two types of response of second-order neurones have been shown: (1) a stable response to stimuli at 10/sec; (2) an unstable response at 1/sec and lower.

When stimuli are applied at 10/sec a given stimulus will give rise to a particular response in the second-order cells and this response can be repeated consistently. Furthermore, the response varies in a regular manner as the stimulus is changed. Increasing the amplitude of the stimulus causes an increase in the mass response of the cells. This may reflect an increase in number of active units and/or an increase in the graded synaptic responses of each. There is evidence that both occur. A large stimulus can excite a cell in the periphery of its receptive field where a small stimulus cannot. Hence, as the stimulus strength is increased, cells whose receptive fields are centred at greater and greater distances from

the point of stimulation will be activated. Increase in stimulus strength can also increase the number of impulses fired by any one second-order cell. The relative size of a stimulus will be greatest where the threshold is lowest; that is, in the centre of a receptive field. Therefore cells, the centres of whose receptive fields are near the stimulus, will be likely to discharge more impulses than those cells whose receptive fields are centred at a distance. There is thus representation of both the strength and position of the stimulus in the patterns of activity of these cells; in other words, information about the stimulus can be transmitted.

The fact that the number of impulses fired by second-order cells is related to the amplitude of the mechanical stimulus means that there must be convergence on to the second-order cells; the primary fibres fire only one impulse each. When stimuli are applied at 10/sec convergence is necessary to achieve threshold. This is shown by the large reduction in threshold that follows a subthreshold conditioning stimulus.

The smallest receptive fields found for second-order cells are smaller than those found for primary units by Armett & Hunsperger (1961). If this is significant it implies that the proportion of the second-order population activated by a stimulus should be smaller than the proportion of the primary population activated by the same stimulus. It has just been argued that the central cells of the active group are likely to discharge more impulses than the peripheral cells. An increase in the ratio of the activity of central units to that of their neighbours and a reduction in the proportion of the population active are features that result from lateral inhibition (e.g. *Limulus* eye, Hartline, Wagner & Ratliff, 1956; the mammalian cochlea, reviewed by Whitfield, 1957). In this instance there is no evidence of lateral inhibition on to the second-order cells, whether it comes from the primary fibres or from the axons of second- or higher-order cells. The results can, however, be explained in terms of the convergence which has been shown to exist. This may be seen more clearly in the next section.

The response of the cells to stimulation at frequencies of 1/sec is entirely different. There is little consistency between input and output. The units, however, can be fired by displacements of about the same size as the thresholds of the most sensitive primary units; this means that the second-order cells are fired when few primary fibres are active. The duration of this activity is long and it is more widely distributed in the cord; it has in some degree a regenerative or explosive character.

The difference in behaviour at these two stimulating frequencies is striking, but it is not difficult to see a possible biological significance. The stable response can transmit information, the explosive response could serve an alerting function. R. M. Eccles (unpublished) has shown fibres

which descend in the spinal cord and which inhibit these cells. This raises the interesting possibility that the function of the cell population at any moment may be determined by signals descending from the brain.

A model

A model is proposed which can explain the transformation of the patterns found in the primary population to those found in the second-order population. The model is based on three observations and two principal assumptions. The observations are that there is convergence of contiguous primary units, that there is no evidence of lateral inhibition at this level and that there are both monosynaptic and polysynaptic connexions between the two populations. The evidence for the last statement is considered by Armett *et al.* (1961) and comes from impulse patterns (see also Hunt & Kuno, 1959) and internal records of synaptic activity (also R. M. Eccles, unpublished). The two assumptions are that the numbers in the two populations are approximately the same and that the polysynaptic connexions are via other cells of the second-order population. There is at present no evidence for a separate group of cells and this assumption is therefore the simplest that can be made.

The model proposed is illustrated in Fig. 13. This illustration is simplified in a number of respects in order that the principle should be clear. The numbers in the lower part of the figure indicate the position of the receptors, if these are assumed to be spaced so that each is equidistant from all its six immediate neighbours. The cells are arranged and numbered in the same way in the top part of the figure. Inputs to each cell are shown not only from the corresponding primary unit but also from the six immediate neighbours; these are all that are shown, but further connexions are visualized. As has been stated, the polysynaptic link is assumed to come from other cells of the population and hence each cell is indicated as receiving connexions from the outputs of its six immediate neighbours.

If the excitability of the cells is low in an organization of this kind, a convergence of say 6 or 7 impulses might be required to excite a cell. This is consistent with the number of primary units needed to be excited in order to excite a second-order cell when stimulated at 10/sec. Under these circumstances the model would tend to show repetitive firing in the centre because of successive convergence of activity first from primary units and then from neighbouring cells. Also, fewer cells than receptors would fire because the outer cells would not receive sufficient convergence.

When these preparations were stimulated at 1/sec, very few primary units had to be activated to fire a second-order cell. If the excitability of the model is increased so that a single primary unit can fire a second-order cell, then the response will spread out in space and on in time without

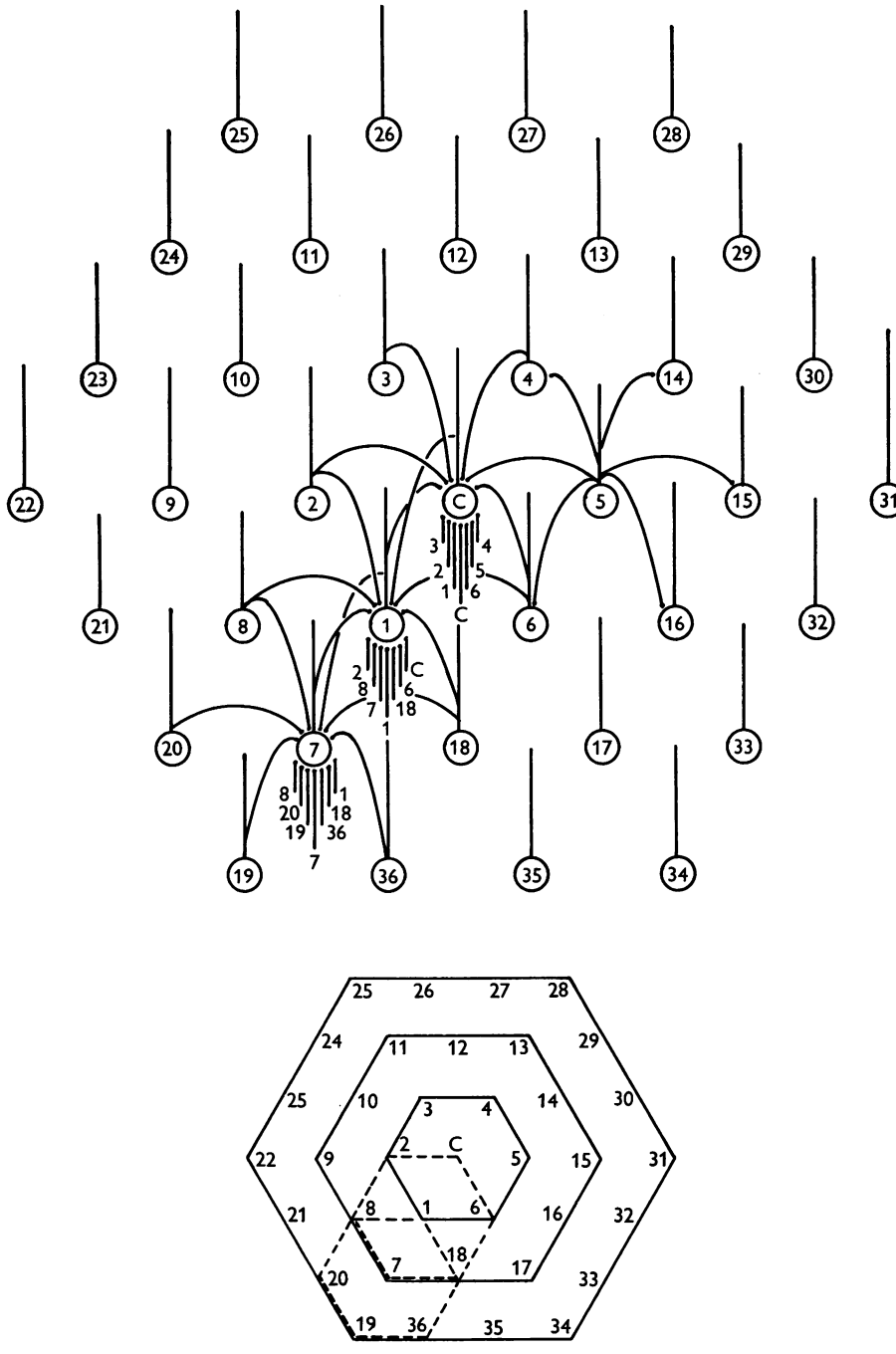

Fig. 13. Model of neuronal organization in relation to the input from mechanical stimulation of the pad. For explanation see text.

limit. The actual response does spread in space and in time but is limited. This limitation is to be expected because the results show that activation causes a decrease in excitability. The instability observed may be partly explained by the fact that any random changes in the cell threshold will be proportionately much bigger if the total change of membrane potential required for excitation is small.

In conclusion, it must be emphasized that the system which has been investigated has been deliberately restricted in the hope of establishing certain principles about the transmission of information in a purely phasic system; one in which the primary units fire only one impulse each in response to a displacement. The system as described is not the whole receptor system of the pad and the part played by receptors having other characteristics is not touched upon. Connexions to the cells from outside the pad have also been ignored.

SUMMARY

1. The object of this investigation was to find out, as far as was possible, how information is carried in the primary receptor neurones and second-order neurones of a phasic system; in this instance a system in which a mechanical stimulus was known to set up only one impulse in any one primary fibre. The pad and lumbo-sacral cord of the cat were used.

2. Single primary units of the system have already been investigated (Armett & Hunsperger, 1961). The response of the whole population was assessed by recording the area of the monophasic action potential in the whole nerve from the pad. The area of this response was closely related to the size of the stimulus. The time course and recovery of the response were noted.

3. When the pad was stimulated mechanically at 10/sec the thresholds and responses of second-order units were very stable. At this repeat frequency the number of impulses fired was usually only one and never more than two or three. The mass response increased steadily with mechanical stimulus strength. The number of impulses fired in response to electrical stimulation of the medial plantar nerve at this frequency also increased with increasing stimulus strength.

4. When the preparation was stimulated mechanically at < 1/sec the responses were very variable and in some instances showed no correlation with stimulus strength. On the average there was a significant correlation between the number of impulses discharged by a second-order cell and the stimulus strength.

5. Receptive fields of second-order cells varied considerably in size ($2{\cdot}5 \times 1{\cdot}5$ mm to 9×9 mm). The smallest were smaller than those of

primary units. The threshold for excitation of the second-order cell was lower in the centre and increased towards the periphery.

6. Experiments were carried out to investigate the pattern of convergence on the second-order cells. These experiments were performed with a conditioning-test technique at 10/sec and the input to the cord was measured in terms of the estimated number of fibres which were active in the primary population. Significant facilitation was seen at intervals of 0–3 msec at all distances between stimuli up to 9 mm apart. At no distance or time was there evidence of inhibition.

7. A model of the pattern of the activity in the primary population has been built up from the values given by Armett & Hunsperger (1961). The relation between the number of active units and the stimulus strength and the time course of monophasic action potentials derived from the model were found to be consistent with the results obtained in this investigation.

8. When the pad is stimulated at 10/sec firing of the second-order cell indicates a critical and constant level of convergence on it. It is concluded that the number of active second-order units must vary with stimulus strength and that the cells in the centre of the array may fire more than once. When the pad is stimulated at low frequencies (< 1/sec) little information can be transmitted. Activity is, however, relatively widespread and lasts up to 40 msec. The cells may, under these conditions, perform some alerting function.

9. A model of the system is proposed. It is based on three observations: convergence, no evidence of lateral inhibition and both mono- and polysynaptic connexions between the populations (Armett *et al.* 1961). The other findings described are consistent with the model.

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